

**REMARKS/ARGUMENTS**

Claims 1-7, 9-16, and 18-22 were rejected under 35 USC 103(a) over WO 90/13285 (Gombotz) in view of US Patent No. 4,470,202 (Buxton). Applicants respectfully traverse the rejection for the following reasons.

The claims of the present invention recite a system and method for preparing small particles by rapidly freezing particles of a drug below the liquid level of a cryogenic liquid, i.e., directly into a freezing environment. The speed of the freezing is important; because the droplets are sprayed directly into a dense cryogenic liquid, they freeze very rapidly very rapidly, do not have time to grow, and small particles result. The density of the cryogenic liquid is important; a more dense cryogenic liquid increases the speed with which the droplets are frozen.

By contrast, Gombotz describes spraying above the level of a liquid. Gombotz does not teach or suggest spraying directly into a liquid. As a result, the particles in Gombotz would have different character than the particles resulting from the present invention – for example, the Gombotz particles would be relatively large larger because they would not freeze as quickly as those prepared using the present invention. For this reason, the present claims are not obvious in view of Gombotz.

Buxton describes a system that gradually freezes droplets. Buxton teaches cooling liquids that have very different densities than the cryogenic liquids used in the present invention. The particles float upward in the system taught by Buxton due to buoyancy derived from the density differences. Gradual freezing would also result in larger particles than those formed according to the present invention, because the time required to float the particles upward gives the particles time to grow. Buxton does not teach or suggest rapidly freezing droplets so as to create small particles. For these reasons, the claims pending in the present application are not obvious over Buxton.

There is no motivation to combine the teaching of Gombotz and Buxton, since one teaches spraying above a liquid surface, and the other teaches spraying below a liquid surface to gradually generate frozen particles. Even if the references were combined, there is no suggestion of a system or method for spraying a drug solution below the surface of a

cryogenic liquid so as to rapidly generate frozen particles. For these reasons, the present claims are not obvious over Gombotz or Buxton, either alone or in combination.

**CONCLUSION**

Based on the foregoing remarks, Applicants believe the present invention now stands in condition for allowance. Early notification thereof is respectfully requested.

Respectfully submitted,

*Elisabeth T Jozwiak*  
Elisabeth T. Jozwiak  
Registration No. 41,101  
Phone: 989-636-2880

P. O. Box 1967  
Midland, MI 48641-1967

ETJ/ab